ENCEPHALOPATHY, COMA AND OTHER ALTERED MENTAL STATUS STATES IN CRITICAL ILLNESS

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Introduction

Patients with critical illness frequently experience alterations in mental status due to global cerebral dysfunction as well as focal neurological injury. These states of altered mental status (AMS) can be due to impaired cognition or impaired consciousness. Patients with an acute and fluctuating global disturbance in cognitive function are said to be in a state of delirium. Global cerebral dysfunction associated with medical illness is often referred to as encephalopathy. When the etiology is known then an etiology-specific term such as hepatic encephalopathy is used. Often there are multiple potential contributing factors and as such a more generic term such as metabolic encephalopathy or critical illness encephalopathy. Impaired consciousness on the other hand can vary from light states of drowsiness to coma. Although terms such as stupor, lethargy and obtundation, have been used to describe various states of arousal, the ambiguity associated with such descriptions has made their utility in clinical medicine less certain.

This clinical review will focus on providing an approach to understanding the various states of altered consciousness as well as discussing the diagnosis and management of three of the most common causes of encephalopathy in the critically ill patient; hypertensive encephalopathy, hepatic encephalopathy and anoxic encephalopathy.

Coma and States of Impaired Consciousness

A. Overview

Consciousness represents a state of neurological function that includes two interrelated domains: arousal and awareness. Arousal is mediated via input from the ascending reticular activating system (ARAS) in the pontine and midbrain tegmentum through the thalamus and to the hemispheric cortex. Awareness on the other hand is dependent on the ability of the aroused cortex to process afferent sensory input and add contextual meaning. Awareness includes memory, perception, motivation and executive function. The transition between states of consciousness can be abrupt such as after a seizure or cardiac arrest or the change may be seamless and represent a continuum of consciousness such as the decline seen in patients with hepatic or renal encephalopathy.

Coma represents the most severe disruption in arousal and awareness. It is differentiated from other conditions that impair consciousness such as syncope or post seizure states by lasting greater than one hour. Comatose patients do not remain in this state indefinitely.
In most patients there is an evolution towards either full recovery or development of persistent states of impaired consciousness such as vegetative state, minimally conscious state, or in the most extreme case, brain death. Coma results from the disruption of the function of both cerebral hemispheres or by the disruption or inactivation of the ARAS.

B. Epidemiology

Coma is common among patients with critical illness. Between 15% and 20% of patients on mechanical ventilation are comatose and increased up to 25% in those patients failing to wean off mechanical ventilation. Among elderly (age >65) patients admitted with critical illness, nearly one third are comatose on admission. Not only is coma frequently seen in patients admitted to the ICU but it is also a powerful predictor of outcome. Among 558 patients admitted to the ICU, Teres et al found that coma was the strongest independent predictor of death and length of stay. In a prospective cohort study of 15, 973 patients, coma developing in the setting of sepsis has been shown to be associated with mortality rates higher than those in comatose trauma patients.

C. Diagnosis

The evaluation and management of the comatose patient begins by initially stabilizing and providing life support measures such as the maintenance of an adequate airway, providing ventilation and supporting cardiovascular function. Once cardiopulmonary stability has been achieved, determining whether the underlying cause of the comatose state is due a structural mass lesion or a metabolic cause is critical.

Structural causes of bihemispheric dysfunction can often be differentiated from brainstem lesions that interrupt the ARAS on the basis of the neurological examination. The ARAS is located in the tegmentum of the pons and midbrain therefore structural lesions at these sites would be expected to disrupt the function of cranial nerves at these locations. Compression of the midbrain is expected to be associated with third nerve palsy (dilated un-reactive pupil), while pontine lesions may be associated with loss of corneal reflexes (5th nerve palsy), loss of lateral rectus function (6th nerve palsy), facial weakness (7th nerve palsy), failure of oculocephalic reflex (8th nerve palsy). Hemispheric, unilateral mass lesions typically cause coma either by increasing intracranial pressure or by inducing a herniation syndrome with subsequent compression of the brainstem. An emergent CT scan of the brain should be done on the comatose patient in order to determine if there is a structural lesion that is amenable to surgical or medical intervention.

Nonstructural disorders produce coma by diffusely depressing cortical or brainstem function thus decreasing arousal mechanisms. A helpful distinguishing feature of metabolic causes of coma is the relative preservation of the papillary reflex with the rare exception being anticholinergic overdose, severe anoxic injury and malingering).
Non-structural causes of coma may be separated into failure of metabolic substrates (hypo or hyperglycemia, hypoxia), metabolic toxemia (hepatic failure, renal failure), electrolyte and acid/base failure (hyponatremia, acidosis, alkalosis), infections (sepsis, CNS infections), endocrine crises (thyroid), and exogenous drugs and toxins (medical and recreational drugs, carbon monoxide). Non convulsive status epilepticus may be associated with coma either on its own or in association with a structural as well as non-structural metabolic disorder. Up to 20% of patients in the ICU with unexplained coma have been shown to be in non-convulsive status epilepticus\textsuperscript{11, 12}. As such, an EEG should be part of the diagnostic work up of all comatose patients.

D. Differential Diagnosis
A number of other clinical states may resemble coma but have significantly different outcomes. These include the minimally conscious state, the vegetative state, akinetic mutism and the locked-in syndrome. Patients with minimally conscious state display a global alteration in consciousness. Elements of arousal persist with intermittent evidence of self or environmental awareness. These patients may follow commands, attend and occasionally speak but inconsistently. The vegetative state is characterized by a global impairment in consciousness but retention of arousal. Although these patients open their eyes spontaneously they do not react in a meaningful way to environmental cues. This state usually results from severe cortical injury with brainstem sparing. A duration of greater than one month is required to characterize it as a persistent vegetative state (PVS). The diagnosis of PVS is not based on a laboratory test but rather on the observations of clinicians with expertise in coma and neurological injury. Akinetic mutism occurs in the setting of injury to the bilateral frontal lobes. It is most often seen after trauma but may occur in the setting of vasospasm affecting the anterior cerebral arteries (ACA) or with embolic strokes in the ACA territory. Clinically these patients manifest with profound deficiency of executive function and inability to initiate movement or speech (apraxia). Typically they do not exhibit any motor or verbal responses to verbal or noxious stimuli. In spite of the motor deficits there is no spasticity or hyperreflexia present. While the previous disorders typically affect hemispheric cortical or subcortical function, the locked-in state is caused by focal injury to the ventral pons. This results in quadriplegia and anarthria but preserved arousal and awareness. The cause is usually ischemic (basilar artery thrombosis) although a similar syndrome may be seen with intracerebral hemorrhage, multiple sclerosis, central pontine myelinolysis and tumors affecting the pons. Locked-in patients have preserved cognitive and sensory function and often are able to communicate with eye blinking or vertical eye movements.

E. Treatment
Treatment of the comatose state depends on the underlying pathophysiology. Coma associated with structural lesions is managed by removing the lesion when ever possible (i.e. removing tumors, evacuating bleeds, decompressing ventricles with hydrocephalus). The specific treatment of intracranial hypertension will not be covered in this review. Non structural disorders are treated by correcting the metabolic disorder whenever possible.
F. Coma Scoring Systems
Several coma scales have been developed to allow health care givers to quantitatively describe the depth of impairment. The most commonly used scale is the Glasgow Coma Scale\textsuperscript{13}. The GCS has been shown to be reliable and reproducible but it has a number of limitations. It is important to note that the scale was initially designed for evaluation of comatose trauma patients. Its utility in patients with coma from metabolic causes or in the setting of vascular disorders is less certain. Patients with aphasia are not accurately assessed by the GCS given the prominent role of speech in the scoring system. By its very nature, endotracheal intubation also limits the GCS to a maximum potential of 11 out of 15 points. In spite of these limitations however, the GCS is still the most utilized coma scale and familiarity with it is essential for intensive care practitioners. Wijdicks has recently developed a coma score with a more extensive neurological evaluation in an effort to address the limitations of the GCS\textsuperscript{14}.

\textbf{Encephalopathy}

Encephalopathy in its most basic terms refers to global cerebral dysfunction. When a known cause is associated with it, the metabolic disorder of note is used to describe the disorder. Although there are numerous causes of metabolic encephalopathy, this review will be limited to three disorders frequently encountered by the neurointensivist; hypertensive encephalopathy, hepatic encephalopathy and hypoxic/anoxic encephalopathy.

\textit{Hypertensive Encephalopathy} is associated with an acute elevation of blood pressure beyond the patient’s autoregulatory range. These patients present with acute headache, nausea, vomiting and visual disturbance. Seizure may also be part of the presenting syndrome. Fundoscopic examination may show arteriolar spasm, exudates, hemorrhages and papilledema in the setting of systemic hypertension. Neuroimaging studies classically show subcortical parieto-occipital edema; ie. posterior leukoencephalopathy [PRES] (figure 1.)

![Figure 1. Posterior Leukoencephalopathy in Hypertensive Encephalopathy](image)

Treatment of hypertensive encephalopathy begins by treating the hypertension. This is a hypertensive emergency and thus requires parenteral antihypertensive therapy with arterial pressure monitoring in an intensive care setting. Untreated, the clinical symptoms may progress to coma and death. Both the clinical and imaging findings tend to reverse with time.
Seizures in the setting of hypertensive crisis do not require the addition of antihypertensive agent but rather the control of blood pressure.

Hepatic encephalopathy is the hallmark of advanced liver failure. Neurological problems result from accumulation of toxins (ammonia is a surrogate marker of multiple toxins- GABA, various branched chain amino acids as well as opioids etc) as well as cerebral edema. The onset of symptoms may be subtle and includes personality change, delirium, drowsiness and progression to coma. Usually exacerbations of encephalopathy are precipitated by acute metabolic change (GI bleed, infections, electrolyte imbalance and medication changes). As the encephalopathy worsens patients with hepatic encephalopathy progress through various stages of clinical decline. Stage 1 is characterized by mental slowness, anxiety, impaired attention and impaired calculation. Stage 2 is associated with a state of lethargy or apathy and personality change. Left untreated, this progresses to stage 3 with worsening lethargy and somnolence and confusion however patients are still capable of responding to verbal stimuli. Stage 4 is characterized by hepatic coma which eventually leads to death unless the patient is treated or undergoes liver transplantation. The earlier the encephalopathy is treated, the better the outcome. As infections are frequently the precipitating cause, diagnosing the source and nature of the infection is essential. Spontaneous peritonitis is frequently one source of infection that is overlooked. Initial antibiotic choice should include vancomycin and a fluoroquinolone. Electrolyte defects need to be corrected (especially potassium). If mechanical ventilation is indicated, set the parameters to induce a mild respiratory alkalosis. In cases of low grade encephalopathy use lactulose to reduce ammonia production in the gut. Lactulose however does not improve survival in advanced hepatic encephalopathy. Late stage liver failure is associated with profound coagulopathy and failure of gluconeogenesis. If active bleeding occurs, correct the coagulopathy with fresh frozen plasma. Continuous glucose infusions may be necessary to correct the hypoglycemia. Cerebral edema precedes death. Monitoring and treating elevated intracranial pressure may prolong life sufficiently to allow for transplantation. Treatment of elevated intracranial pressure with mannitol needs to be done with caution as it may result in significant dehydration and fluid shifts which can worsen the encephalopathy. Hypertonic saline may be a viable alternative to mannitol. Transplantation is usually the only viable option.

Anoxic encephalopathy from cardiac arrest is an ever increasing problem with the advent of automatic electrical defibrillators in the public domain. In spite of improved rates of cardiac resuscitation over the past 10 years, the prevalence of severe anoxic encephalopathy has not decreased. Out of hospital arrests occur n 100-120/100,000 per year. The incidence of cardiac arrest in the hospital is about 0.17 events per hospital bed per year. Rapidly restoring cerebral blood flow has the most impact on functional survival and thus has lead to the concept of providing cardio-cerebral-resuscitation during resuscitation. Increased focus has been on providing highly effective CPR early then securing an airway.
Even after return of spontaneous circulation is achieved, the brain experiences a relative state of no-reflow in the microcirculation which lasts from 2-48 hours. Delayed neuronal death due to multiple cascades ensues eventually leading to the patients dying or being left in a severely impaired neurological state. The leading cause of death among patients surviving the initial cardiac arrest is from severe neurological injury. Induced moderate hypothermia has been demonstrated in numerous preclinical models to be highly effective in reducing multiorgan injury associated with cardiac arrest.

Two pivotal randomized clinical trials evaluated the efficacy of induced systemic hypothermia following cardiac arrest. The HACA study randomized patients that had achieved return of spontaneous circulation (ROSC) after out of hospital witnessed cardiac arrest (ventricular fibrillation or pulseless ventricular tachycardia) to induced systemic hypothermia with a target core temperature of 32-33°C versus standard best medical care at normothermia. Of note only patients with ROSC within 60 minutes of collapse were included. All the cooling was done after arrival to the hospital. Hypothermia was maintained for 24 hours followed by passive rewarming. A total of 273 patients were randomized to either hypothermia (136) or normothermia (137). There were no significant adverse events associated with hypothermia treatment except for bradycardia. At six months, 53% of the hypothermia treated patients had a favorable outcome compared to 35% of the controls. A smaller but similar study was also reported from Australia in which 77 patients with ROSC after witnessed VT/VF arrest were randomized to hypothermia (43) versus standard normothermic care (34). These patients had the hypothermia therapy initiated in the ambulance (topical ice and cooling baths) and maintained in the ICU for 12 hours followed by active rewarming. Favorable outcomes were seen in 49% of the hypothermia treated patients compared with 26% of the controls. Based on the results of these studies as well as subsequent observational cohort studies, the American Heart Association as well as the International Liaison Committee on Resuscitation has advised that unresponsive (comatose) survivors of cardiac arrest from VT/VF should be considered for hypothermia therapy. They also advised that this treatment may be considered for survivors of cardiac arrest associated with asystole or pulseless electrical activity.

Implementing post arrest hypothermia therapy as a standard treatment however has proven to be much more challenging than proving its benefit. There continues to be a general lack of knowledge regarding the beneficial effects of this form of therapy in spite of the AHA and ILCOR guidelines. Practitioners of multiple disciplines have sites lack of evidence, lack of AHA/ACLS guidelines and technical difficulty as reasons for not utilizing this form of therapy. Implementation of therapeutic hypothermia requires a multidisciplinary team. As such it is critical to have representation from emergency medicine, cardiology, critical care medicine and if available, neurocritical care medicine. Nursing input and collaboration is essential to the success of any new therapeutic protocol. Developing an institutional protocol is also paramount to the success of the treatment. Hypothermia can be easily induced with the use of hypothermic intravenous fluids. Bernard et al demonstrated that patients treated with an infusion of 30 ml/kg of hypothermic (2-4°C) Lactated Ringers solution had a reduction in core temperature of approximately 1.6°C in 30 minutes.
Completing the induction phase of cooling to achieve a target temperature of 32C currently requires active cooling with mechanical devices. Both surface and intravascular cooling devices are commercially available and routinely used for this purpose although it is worthy to note that this application is “off-label” use since currently the US Food and Drug Administration has not approved any mechanical device (surface or intravascular) for the induction and maintenance of therapeutic hypothermia.

Appropriate patient selection is important. Currently this form of therapy is advised only for non-responding or comatose survivors of cardiac arrest. This typically includes patients with GCS<8 (non-purposeful motor response to pain). Early induction in the field by the EMS/paramedic first responders may accelerate the rate of cooling. Attached is a protocol that has been developed for use by EMS and Emergency Medicine personnel at Duke University Medical Center. It can be modified to suit individual institutional needs. Once a patient is in hospital then completion of the induction phase and maintenance of hypothermia may follow. We have attached the hypothermia protocol developed for Duke University Medical Center. Both surface and vascular cooling options are included in order to account for variable methods of hypothermia maintenance.
DURHAM COUNTY EMS HYPOTHERMIA PROTOCOL

Non-traumatic Cardiac Arrest

CPR Performed for 60 minutes or less

ROSC (Return of Spontaneous Circulation)

Patient Intubated, GCS less than 9 (no purposeful movement), No contraindications (known DNR status, age less than 18, SBP<80 mmHg); ER aware that post arrest hypothermia patient in route.

Expose entire body, apply ice packs to axilla and groin

Start Peripheral or Intraosseous IV

Start Infusion of 2 Liters of Iced Lactated Ringer’s Solution, wide open, maintain SBP>80 mmHg

Arrive in ED, perform brief neuro exam. Abort hypothermia therapy if GCS>9 (purposeful motor function or following commands). Continue 4°C Normal Saline until a total of 30ml/kg (unless core temperature is 32°C).

Place Foley Catheter with Temp Probe, document vital signs including temp q15 min. Order post arrest lab bundle on CPOE. Continue to cool with iced-saline as maintenance fluid. Paralyze patient with non-depolarizing muscle relaxant, monitor with train-of-4 (goal of 1:4) and sedate patient with Midazolam or Propofol and provide analgesia with fentanyl. Review documented initial rhythm provided by EMS, evaluate EKG and cardiac enzymes. Patient determined to be a candidate for acute coronary intervention; YES or NO

Contact 4200 Rapid-Response Hypothermia-Team (970-6131) regarding bed availability immediately to determine disposition; Notify Operations Administrator to help with bed allocation. Femoral cooling catheter (ICY-Catheter) will be inserted.

If ICU bed (4200 or 8200) is not immediately available, cooling machine will be brought to ED and connected to catheter for completion of induction and maintenance of hypothermia

Transport pt. to CCU or cath. Lab; Begin cooling in ED if CCU bed not immediately available and set target temperature to 32°C. Continue with paralytic and sedative/analgesic protocol

Transport pt. to 4200 (NICU) or 8200 (MICU), provide vascular cooling (set temp to 32°C) for 24hours; monitor with EEG, BIS and TOF. Continue sedation and analgesic protocol. Cooling patients on 8200 to be followed in consult by Hypothermia Team until 24 hours following rewarming.

Hypothermia after Cardiac Arrest
Cooling Protocol
Duke University Medical Center
Inclusion Criteria:
1. Cardiac arrest with return of spontaneous circulation (all cases of VT/VF and PEA/Asystole if non of the exclusion criteria apply)
2. Patients 18 years or older.
4. Endotracheal intubation with mechanical ventilation.
5. Blood pressure can be maintained: SBP >90 or MAP >60 either spontaneously or with fluid and pressors.
6. Ability to initiate cooling within 6 hours of arrest
7. 
   **NOTE 1: Cooling is now suggested as a treatment option by ACLS guidelines. This is NOT part of a study. NO informed consent is needed.**
8. 
   **NOTE 2: Induced hypothermia after PEA, asystolic, or in-hospital arrest has not been studied in randomized trials. Inclusion of such cases must be decided on an individual basis.**

Exclusion Criteria:
1. A non-cardiac arrest etiology for coma (e.g. drug overdose, major head trauma, stroke, overt status epilepticus)
2. Known down time >30 minutes prior to initiation of ACLS (no specific limit on time of resuscitation effort).
3. Greater than 6 hours since onset of arrest.
5. Ongoing severe shock with likely recurrent arrest / CPR.
7. Not intubated.
8. Less than 18 years old.
9. Patients with known bleeding diathesis or with active ongoing bleeding.
10. Systemic infection / sepsis.
11. DNR or DNI status.

Protocol:
**Time to cooling is critical. Proceed through initial steps as quickly as possible.**

1. **ED assessment** and stabilization:
   - Intubation
   - Arterial line
   - Chem 7, CBC, PT/PTT, fibrinogen, d-dimer, CK/MB/troponin, hCG
   - ABG
   - EKG (baseline post CPR)
   - CXR
   - Noncontrast head CT if evidence of head trauma (r/o ICH)
2. Patients may receive chemical thrombolysis, antiplatelet agents, or anticoagulants if deemed necessary in the treatment of the primary cardiac condition.
3. Document post resuscitation **neurologic status via** GCS score
   i. Best eye response (1-4) ____
      1. No eye opening
      2. Eye opening to pain
      3. Eye opening to verbal command
      4. Eyes open spontaneously
   ii. Best verbal response (1-5) ____
      1. No verbal response
      2. Incomprehensible sounds
      3. Inappropriate words
      4. Confused
      5. Oriented
   iii. Best motor response (1-6) ____
      1. No motor response
      2. Extension to pain
      3. Flexion to pain
      4. Withdrawal from pain
      5. Localizing pain
      6. Obeys commands
   iv. Total GCS: ____ (should be < 9 for cooling)

4. Administer **paralytic**: Patients must be paralyzed while cooled. Never paralyze a patient who is not adequately sedated. We recommend:
   - Cisatracurium (Nimbex): 0.1 mg/kg bolus
   - Cisatracurium (Nimbex): 1 mcg/kg/hr (range 1-3)
   - Use Train-of-Four to adjust Nimbex dosing; goal TOF level is 1 in 4.

5. **Cold saline infusion**:
   - NS at 4°C: 30 ml/kg bolus over 30 minutes – start as early as possible once decision to cool is made

6. Assess and treat patient for **comfort**: Administer narcotic to appropriate comfort level. Even if comatose provide narcotic for comfort. We recommend:
   - Fentanyl 50-100 mcg/kg IV push
   - Fentanyl 25-75 mcg/hr, adjust prn

7. Assess and treat patient for **sedation**: Administer benzodiazepine for appropriate sedation level. Even if comatose provide benzo for sedation. We recommend:
   - Midazolam (Versed) 2-4 mg IV push
   - Midazolam 2-4 mg/hr to start, adjust prn (0.125 mg/kg/hr is a moderate dose)
   - If BIS is available, titrate sedative to achieve BIS score of 40-60.

8. **Temperature monitoring**:
   - Place bladder temperature probe catheter (preferred; most accurate method)
Secondary measures of temperature (tympanic membrane or rectal) should be checked occasionally as bladder probes can fail and are less accurate in setting of oliguria.

9. **Intravascular Cooling Protocol**
   a. Insert Icy™ Cooling catheter into the femoral vein using Seldinger technique and central venous insertion bundle—do not flush catheter balloon ports (brown tipped ports) prior to insertion into the vein.
   b. While catheter is being inserted prime cooling tubing and initialize the CoolGard™ as per operating manual; set target temperature to 32°C and cooling rate to maximum.
   c. Connect bladder temperature port to the CoolGard™
   d. Once catheter is in vein flush the balloon ports with saline then attach to cooling tubing from the CoolGard cooling device.
   e. Keep patient at 32°C for 24 hours.

10. **Active external cooling Protocol (If intravascular system not available):**
    
    - Place ice packs to the armpits, neck, torso, groin, and limbs. Also apply 2 cooling blankets (1 above and 1 below the patient) or if using Arctic Sun, apply blankets as per operating manual. Change ice packs as needed to keep cool. Target time to reach temperature goal of 32°C is <3 hours.
    - Once the patient reaches 32°C remove the ice packs, and then one cooling blanket (if using water cooled pads) if necessary. Maintain a target temperature of 32-33°C by adjusting ice and blankets.
    - Cool for 24 hours once target temperature (32-33°C) is reached.

11. **Neurology consultation with request for EEG monitoring x 48 hours**

12. **Labs:** q8hr during cooling, with Chem7 q4hr during rewarming
    
    - CBC, Chem7, PT/PTT, ABG
    
    **All ABG measurements must be analyzed at the patient’s actual body temperature – write temp on slips and make this clear to the stat lab**
    **Do NOT correct mild hypokalemia (goal to keep K at >3.0mmol/L) as cooling causes influx of potassium into cells; during rewarming hyperkalemia can occur**
    **Mild increases in amylase and lipase are common**

13. **Management of shivering:**
    
    - Consider increasing muscle relaxant (TOF 0-1/4) and adding further sedatives if necessary; (consider adding dexmedetomidine).

14. **Interventions** while cooling:
    
    - Usual cardiac and medical care
    - DVT prophylaxis with low molecular weight heparin
    - GI prophylaxis
15. **Blood pressure** control
   - Maintain MAP >70 with pressors as clinically indicated: (given cerebral injury, relatively higher MAP is advised if possible).
   - Maintain MAP <110 with BP agents as clinically indicated.
   - For MAP 70-110, clinical judgment is advised. Most patients will be post-MI with ventricular arrhythmia, so beta-blockers and ACEI are likely indicated.

16. **Rewarming**: Goal is slow controlled rewarming over about 10-12 hours. Begin after 24 hours at goal temperature.
   a. Keep patient’s cooling catheter connected to CoolGard (if this device used)
   b. If surface cooling is being used, keep blankets on the patient
   c. Set rewarming rate at 0.5°C / hour
   d. Once patient’s temperature has reached 37°C, remove cooling catheter or cooling blankets.
   e. Maintain patient at 37°C

17. Stop paralytics once patient has been rewarmed to 36.5°C

18. Monitor for **potential complications**:
   a. Bleeding: coagulation cascade is impaired with hypothermia
   b. Infection: immune system is impaired with hypothermia
   c. Arrhythmia: Osborne or camel waves often seen on EKG with rewarming. Transient atrial and ventricular arrhythmias are common. Warming is optimal treatment for severe arrhythmia. Bretylium is classically used but is not available. Procainamide should not be used due to risk of precipitating VF.
   d. Status epilepticus: Usually due to underlying brain injury from arrest.
   e. Hyperkalemia / Potassium balance: Typically during rewarming, as increased temperature causes shift of K out of cells.

Citations:
   - AHA 2005 Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

REFERENCES


